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First Named Inventor:	CANTOR, ADAM S.		
Application No.:	09/965610	Confirmation No.:	8132
Filed:	September 26, 2001	Group Art Unit	1611
Title:	COMPOSITION FOR THE TRANSDERMAL DELIVERY OF FENTANYL		

BRIEF ON APPEAL

Mail Stop: Appeal Brief-Patents
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9/24/2008 /Chris Johnson/

Date Signed by: Chris Johnson

Dear Sir:

This is an appeal from the Office Action mailed on March 24, 2008, in light of the Advisory Action mailed July 7, 2008, finally rejecting claims 1-9, 16-18, 28-31, 35-37, 39-47 and 52-54.

Fees

☒ Any required fee under 37 CFR § 41.20(b)(2) will be made at the time of submission via EFS-Web. In the event fees are not or cannot be paid at the time of EFS-Web submission, please charge any fees under 37 CFR § 1.17 which may be required to Deposit Account No. 13-3723.

☒ Please charge any additional fees associated with the prosecution of this application to Deposit Account No. 13-3723. This authorization includes the fee for any necessary extension of time under 37 CFR § 1.136(a). To the extent any such extension should become necessary, it is hereby requested.

☒ Please credit any overpayment to the same deposit account.

A Notice of Appeal in this application was mailed on June 24, 2008, and was received in the USPTO on June 24, 2008.

Appellants request the opportunity for a personal appearance before the Board of Appeals to argue the issues of this appeal. The fee for the personal appearance will be timely paid upon receipt of the Examiner's Answer.

REAL PARTY IN INTEREST

The real party in interest is 3M Company (formerly known as Minnesota Mining and Manufacturing Company) of St. Paul, Minnesota and its affiliate 3M Innovative Properties Company of St. Paul, Minnesota.

RELATED APPEALS AND INTERFERENCES

Appellants are unaware of any related appeals or interferences.

Claims 55-91 have been withdrawn but are the subject of a co-pending divisional application. These claims were added for the purpose of provoking an interference with Venkatraman et al., U.S.S.N. 10/850,865, entitled "Transdermal Administration of Fentanyl and Analogs Thereof."

STATUS OF CLAIMS

Claims 1-9, 16-18, 28-31, 35-37 and 39-91 are pending. Claims 48-51 and 55-91 are withdrawn. Claims 1-9, 16-18, 28-31, 35-37, 39-47 and 52-54 stand rejected.

STATUS OF AMENDMENTS

No amendments have been filed after the final rejection.

SUMMARY OF CLAIMED SUBJECT MATTER

The claims at issue concern a transdermal composition comprising an acrylate adhesive copolymer and fentanyl in an amount of about 8 to 30% by weight of the total weight of the composition, the composition being free of undissolved fentanyl.

GROUND OF REJECTION TO BE REVIEWED ON APPEAL

Ground of Rejection

Claims 1-9, 16-18, 28-31, 35-37, 39-47 and 52-54 stand rejected under 35 USC § 103(a) as purportedly unpatentable over the teachings of WO 96/08229 ('229) by itself or in view of US 5,993,849 ('849).

ARGUMENT

Ground of Rejection

Claims 1-9, 16-18, 28-31, 35-37, 39-47 and 52-54 stand rejected under 35 USC § 103(a) as purportedly unpatentable over the teachings of WO 96/08229 ('229) by itself or in view of US 5,993,849 ('849).

The '229 disclosure is only very general at best with respect to a transdermal formulation containing fentanyl, and the otherwise general disclosure of the amount of drug that can be present, given the myriad of drugs disclosed in the '229 publication and the lack of any emphasis on fentanyl, underscores the insufficiency of this teaching in respect to the pending claims which are directed to transdermal formulations containing a relatively high concentration of fentanyl. As the Examiner recognizes, the '229 publication specifically illustrates delivery of nicotine. It is noteworthy that the Examiner concedes that the '229 publication fails to "specifically exemplify fentanyl". In fact, the only mention of fentanyl is on page 10 (out of 83 pages total) in a paragraph that appears to be an attempt to list almost any and every type of drug. It is asserted that the '229 publication does not lead one skilled in the art to a finding that 8-30% fentanyl by weight would fully dissolve in the claimed formulations.

The alleged equivalency of nicotine and fentanyl which the Examiner points to in the '849 publication does not remedy this deficiency in the '229 publication. Nicotine and fentanyl are dissimilar in more respects than they are similar, and again it is underscored that nicotine is not even a solid at room temperature. Moreover, the only mention of fentanyl in the '849 publication is in claim 10 which lists fentanyl and nicotine as members of a Markush group including other drugs as well including for example disparate drugs such as "diverse peptides". Happenstance mention of both fentanyl and nicotine in a diverse list of drugs simply does not support the Examiner's alleged equivalency of fentanyl and nicotine. And, again contrary to the Examiner's assertion, it is not understood how Naik et al. which compares bioavailability and pharmacokinetics of nicotine and fentanyl teaches anything about a formulation containing an acrylate copolymer and a high loading of dissolved fentanyl.

Finally, Roy et al. is very pertinent to the allowability of the instant claims. This publication speaks directly to fentanyl/acrylate copolymer formulations. Importantly, this

publication discloses the fact that formulations containing over 4% fentanyl had undissolved fentanyl particles in addition to dissolved fentanyl. It is very undesirable to have both dissolved and undissolved drug in a transdermal patch. Thus Roy et al. is a clear teaching away from the formulations of the instant invention.

Applicants would like correct a possible misunderstanding by the Examiner relative to Roy et al.. The sole acrylate adhesive disclosed in Roy et al., namely "Gelva 737", is believed by Applicants to be a copolymer containing 72% 2-ethylhexyl acrylate and 28% vinyl acetate. As such, contrary to the Examiner's apparent assertion in the Advisory Action, that copolymer meets the limitations of the copolymer recited in for example Claim 1 of the instant application. Nonetheless, the language at the end of that claim "wherein the composition is free of undissolved fentanyl" serves to exclude any formulation where the combination of copolymer and the amount of fentanyl are such that there is undissolved fentanyl in the formulation. If anything, the fact the acrylate disclosed in Roy et al. meets the limitations of the copolymer recited in instant Claim 1 further underscores the allowability of that claim.

As all pending claims directly or indirectly require presence of fentanyl in an amount of about 8-30% by weight and further require the composition be free of undissolved fentanyl, it is submitted that all pending claims are allowable.

Applicants assert that the rejection of claims 1-9, 16-18, 28-31, 35-37, 39-47 and 52-54 under 35 USC § 103(a) as purportedly unpatentable over the teachings of WO 96/08229 ('229) by itself or in view of US 5,993,849 ('849) should be reversed.

CONCLUSION

For the foregoing reasons, appellants respectfully submit that the Examiner has erred in rejecting this application. Please reverse the Examiner on the Examiner's ground of rejection.

Respectfully submitted,

September 23, 2008
Date

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CLAIMS APPENDIX

Listing of Claims

1. (Previously presented) A transdermal drug delivery composition comprising:

(a) a copolymer comprising

(i) one or more A monomers selected from the group consisting of alkyl acrylates containing 4 to 12 carbon atoms in the alkyl group and alkyl methacrylates containing 4 to 12 carbon atoms in the alkyl group; and

(ii) one or more ethylenically unsaturated B monomers copolymerizable with the A monomer; and

(b) about 8% to about 30% by weight fentanyl based on the total weight of the composition;

wherein the composition is free of undissolved fentanyl.

2. (Original) The composition of claim 1 wherein the A monomer is selected from the group consisting of isooctyl acrylate, 2-ethylhexyl acrylate, butyl acrylate, and cyclohexyl acrylate.

3. (Original) The composition of claim 1 wherein the A monomer is isooctyl acrylate.

4. (Original) The composition of claim 1 wherein the B monomer is selected from the group consisting of 2-hydroxyethyl acrylate, 2-hydroxyethyl methacrylate, glyceryl acrylate, N,N-diethylacrylamide, 2-ethoxyethoxyethyl acrylate, 2-ethoxyethyl acrylate, tetrahydrofurfuryl acrylate, acrylic acid, acrylamide, vinyl acetate, N-vinyl pyrrolidone and mixtures thereof.

5. (Original) The composition of claim 1 wherein the B monomer is 2-hydroxyethyl acrylate.

6. (Original) The composition of claim 5 wherein the copolymer comprises from about 5% to about 45% of 2-hydroxyethyl acrylate by weight based on the total weight of all monomers in the copolymer.

7. (Original) The composition of claim 1 wherein the copolymer further comprises a macromonomer.

8. (Original) The composition of claim 7 wherein the macromonomer is a functionally terminated polymethylmethacrylate.

9. (Original) The composition of claim 7 wherein the copolymer contains from about 1% to about 6% of macromonomer by weight based on the total weight of all monomers in the copolymer.

10-15. (Canceled).

16. (Original) The composition of claim 1 wherein the concentration of fentanyl in said transdermal drug delivery composition is from about 12% to about 24% by weight.

17. (Original) The composition of claim 7 wherein the copolymer comprises from about 50 to about 94% isooctyl acrylate, about 5% to about 40% 2-hydroxyethyl acrylate, about 1% to about 6% macromonomer, and 0% to about 20% vinyl acetate by weight.

18. (Original) The composition of claim 7 wherein the copolymer comprises from about 52% to about 60% isooctyl acrylate, about 35% to about 40% 2-hydroxyethyl acrylate, about 1% to about 4% macromonomer, and 0% to about 10% vinyl acetate by weight.

19-27. (Canceled).

28. (Original) A method of treating in a mammal a condition capable of treatment by fentanyl comprising the steps of:

(a) providing a composition according to claim 1;

(b) placing the composition on the skin of a mammal; and

(c) allowing the composition to remain on the skin for a time sufficient to establish or maintain a therapeutically effective blood level of fentanyl in the mammal.

29. (Original) A method of providing analgesia to a mammal comprising the steps of:

(a) providing a composition according to claim 1;

(b) placing the composition on the skin of a mammal; and

(c) placing the composition to remain on the skin for a time sufficient to establish or maintain an analgesically effective blood level of fentanyl in the mammal.

30. (Previously presented) A method of providing sustained analgesia to a mammal comprising delivering fentanyl to a mammal via a transdermal drug delivery device in an amount of about 0.5 to about 5.0 mg/day thereby causing the serum concentration of fentanyl in the mammal to be about 0.2 to about 10 ng/mL for a period of time from about 4 to about 14 days, wherein the device includes a composition according to claim 1.

31. (Original) The method of claim 30 wherein the fentanyl is delivered in an amount of 0.5 to 2.5 mg/day, the serum concentration of fentanyl in the mammal is about 0.3 to about 4 ng/mL, and the period of time is from about 6 to about 8 days.

32-34. (Canceled).

35. (Previously presented) A transdermal drug delivery composition comprising:

(a) a copolymer comprising:

(i) one or more A monomers selected from the group consisting of isooctyl acrylate, 2-ethylhexyl acrylate, butyl acrylate, and cyclohexyl acrylate; and

(ii) one or more ethylenically unsaturated B monomers copolymerizable with the A monomer; wherein the B monomers are selected from the group consisting of 2-hydroxyethyl acrylate, 2-hydroxyethyl methacrylate, glyceryl acrylate, N,N-diethylacrylamide, 2-ethoxyethoxyethyl acrylate, 2-ethoxyethyl acrylate, tetrahydrofurfuryl acrylate, acrylic acid, acrylamide, vinyl acetate, N-vinyl pyrrolidone and mixtures thereof; and

(b) about 8% to about 30% by weight fentanyl based on the total weight of the composition;

wherein the composition is free of undissolved fentanyl.

36. (Previously presented) A transdermal drug delivery composition comprising:

(a) a copolymer comprising:

(i) one or more A monomers selected from the group consisting of isooctyl acrylate, 2-ethylhexyl acrylate, butyl acrylate, and cyclohexyl acrylate; and

(ii) about 5% to about 45% of one or more ethylenically unsaturated B monomers copolymerizable with the A monomer; wherein the B monomers are selected from the group consisting of 2-hydroxyethyl acrylate, 2-hydroxyethyl methacrylate, glyceryl acrylate, N,N-diethylacrylamide, 2-ethoxyethoxyethyl acrylate, 2-ethoxyethyl acrylate, tetrahydrofurfuryl acrylate, acrylic acid, acrylamide, vinyl acetate, N-vinyl pyrrolidone and mixtures thereof; and

(b) about 8% to about 30% by weight fentanyl based on the total weight of the composition;

wherein the composition is free of undissolved fentanyl.

37. (Previously presented) A transdermal drug delivery composition comprising:

(a) a copolymer comprising

(i) one or more A monomers selected from the group consisting of isooctyl acrylate, 2-ethylhexyl acrylate, butyl acrylate, and cyclohexyl acrylate; and

(ii) about 5% to about 45% of one or more ethylenically unsaturated B monomers copolymerizable with the A monomer, wherein at least one B monomer is 2-hydroxyethyl acrylate; and

(b) about 8% to about 30% by weight fentanyl based on the total weight of the composition;

wherein the composition is free of undissolved fentanyl; and wherein the drug delivery device delivers fentanyl to a mammal via a transdermal drug delivery device in an amount of about 0.5 to about 5.0 mg/day thereby causing the serum concentration of fentanyl in the mammal to be about 0.2 to about 10 ng/mL for a period of time from about 4 to about 14 days.

38. (Canceled).

39. (Previously presented). The composition of claim 1 wherein the composition further comprises a delivery enhancing adjuvant.

40. (Previously presented). The composition of claim 39 wherein the delivery enhancing adjuvant is selected from the group consisting of alkane polyols, fatty acids, fatty acid esters, fatty alcohols, terpenes, C_5-C_{18} alkyl esters of a carboxylic acid, and mixtures thereof.

41. (Previously presented). The composition of claim 39 wherein the delivery enhancing adjuvant is selected from the group consisting of ethyl oleate, isopropyl myristate, glycerol, tetraglycol, methyl laurate, N,N-dimethyldodecylamine N-oxide, limonene, terpineol, tetraethylene glycol, menthol, and mixtures thereof.

42. (Previously presented). The composition of claim 39 wherein the concentration of the delivery enhancing adjuvant is from about 5% to about 40% by weight based on the total weight of the composition.

43. (Previously presented). The composition of claim 39 wherein the skin permeation enhancer is tetraglycol.

44. (Previously presented). The composition of claim 39 wherein the skin permeation enhancer is methyl laurate.

45. (Previously presented). The composition of claim 17 wherein the concentration of fentanyl is from about 12% to about 22% by weight, wherein the composition further comprises about 15% to about 35% by weight of a permeation enhancer selected from the group consisting of methyl laurate, tetraglycol, and mixtures thereof.

46. (Previously presented). The composition of claim 45 wherein the concentration of fentanyl is from about 12% to about 17% by weight and the concentration of methyl laurate is from about 20% to about 35% by weight.

47. (Previously presented). The composition of claim 45 wherein the concentration of fentanyl is from about 15% to about 22% by weight and the concentration of tetraglycol is from about 15% to about 25% by weight.

48. (Withdrawn). A pressure sensitive adhesive composition for the transdermal delivery of fentanyl comprising

(a) an acrylate polymer;

(b) about 8% to about 30% by weight fentanyl based on the total weight of the composition; and

(c) a delivery enhancing adjuvant selected from the group consisting of methyl laurate, tetraglycol, and mixtures thereof;

wherein the composition is free of undissolved fentanyl.

49. (Withdrawn). The composition of claim 48 wherein the concentration of delivery enhancing adjuvant is from about 5% to about 40% by weight based on the total weight of the composition.

50. (Withdrawn). The composition of claim 48 wherein the acrylate polymer comprises:

(a) one or more A monomers selected from the group consisting of alkyl acrylates containing 4 to 12 carbon atoms in the alkyl group and alkyl methacrylates containing 4 to 12 carbon atoms in the alkyl group; and

(b) one or more ethylenically unsaturated B monomers copolymerizable with the A monomer.

51. (Withdrawn). The composition of claim 50 wherein the B monomer is selected from the group consisting of 2-hydroxyethyl acrylate, 2-hydroxyethyl methacrylate, glyceryl acrylate,

N,N-diethyacrylamide, 2-ethoxyethoxyethyl acrylate, 2-ethoxyethyl acrylate, tetrahydrofurfuryl acrylate, N-vinyl pyrrolidone and mixtures thereof.

52. (Previously presented). A device for the transdermal delivery of fentanyl comprising a backing and a composition according to claim 1, said composition being adhered to one surface of the backing.

53. (Previously presented). The composition of claim 39 wherein the delivery enhancing adjuvant is a skin permeation enhancer.

54. (Previously presented). A transdermal drug delivery composition comprising

(a) a copolymer comprising

(i) one or more A monomers selected from the group consisting of isooctyl acrylate, 2-ethylhexyl acrylate, butyl acrylate, and cyclohexyl acrylate; and

(ii) about 5% to about 45% of one or more ethylenically unsaturated B monomers copolymerizable with the A monomer; wherein at least one B monomer is 2-hydroxyethyl acrylate; and

(b) about 8% to about 30% by weight fentanyl based on the total weight of the composition; and

(c) a delivery enhancing adjuvant selected from the group consisting of methyl laurate, tetraglycol, and mixtures thereof;

wherein the composition is substantially free of undissolved fentanyl.

55. (Withdrawn) A transdermal patch for administering fentanyl through the skin comprising: (a) a backing layer; (b) a reservoir disposed on the backing layer, at least the skin contacting surface of said reservoir being adhesive; said reservoir comprising a single phase polymeric composition free of undissolved components containing an amount of fentanyl sufficient to induce and maintain analgesia in a human for at least three days.

56. (Withdrawn) The patch of claim 55 which is bioequivalent to DURAGESIC®

transdermal fentanyl system.

57. (Withdrawn) The patch of claim 55 wherein said reservoir is formed from an adhesive.

58. (Withdrawn) The patch of claim 55 or 57 wherein said patch exhibits a normalized C_{max} of about 16.8 to 18.7 ng/mL-mg/hr.

59. (Withdrawn) The patch of claim 55 or 57 wherein said patch exhibits a standardized C_{max} of about 0.14 to about 0.17 ng/mL/cm^2.

60. (Withdrawn) The patch of claim 57 wherein the patch exhibits a steady state drug flux of about 8.2 to 8.9 μg/cm^2/hr.

61. (Withdrawn) The patch of claim 55 wherein said reservoir comprises an amount of dissolved fentanyl sufficient to induce and maintain analgesia for about 4-14 days.

62. (Withdrawn) The patch of claim 55 wherein said reservoir comprises an amount of dissolved fentanyl sufficient to induce and maintain analgesia for about 6-8 days.

63. (Withdrawn) The patch of claim 55 wherein fentanyl has a solubility of about 8-30% by weight.

64. (Withdrawn) The patch of claim 55 wherein fentanyl has a solubility of about 12-24% by weight.

65. (Withdrawn) The patch of claim 61 wherein the reservoir comprises about 0.84 to 3.56 mg/cm^{2}of fentanyl base.

66. (Withdrawn) The patch of claim 65 wherein the reservoir comprises about 0.84 to 1.72 mg/cm^2 of fentanyl base.

67. (Withdrawn) The patch of claim 61 wherein the reservoir has a dry coating weight of about 10 to 12 mg/cm^2.

68. (Withdrawn) The patch of claim 57 wherein said adhesive is a polyacrylate adhesive.

69. (Withdrawn) The patch of claim 68 wherein said polyacrylate adhesive has a T_g less than -10^o C.

70. (Withdrawn) The patch of claim 68 wherein the reservoir comprises about 0.84 to 3.56 mg/cm^{2}of fentanyl base.

71. (Withdrawn) The patch of claim 70 wherein the reservoir comprises about 0.84 to 1.72 mg/cm^2 of fentanyl base.

72. (Withdrawn) The patch of claim 68 wherein the reservoir has a dry coating weight of about 10 to 12 mg/cm^2.

73. (Withdrawn) The patch of claim 61 or claim 68 wherein the reservoir further comprises an enhancer.

74. (Withdrawn) The patch of any one of claims 55, 61 or 68, wherein the backing layer comprises a polymer selected from the group consisting of polyethylene, polyethylene terephthalate, ethylene-vinyl acetate copolymer, and polyurethane.

75. (Withdrawn) The patch of claim 74, wherein the backing layer comprises low density polyethylene or high density polyethylene.

76. (Withdrawn) The patch of claim 75, wherein the backing layer comprises low density polyethylene.

77. (Withdrawn) The patch of claim 74 wherein the backing layer has a thickness of about 0.05 mm.

78. (Withdrawn) A transdermal patch for administering fentanyl, comprising an adhesive fentanyl reservoir on a backing layer; said reservoir comprising a single phase polymeric composition free of undissolved components containing a polyacrylate adhesive having sufficient solubility for fentanyl to contain dissolved fentanyl in an amount sufficient to induce and maintain analgesia in a human for at least three days, said patch exhibiting a normalized C_{max} of about 16.8 to 18.7 ng/mL-mg/hr.

79. (Withdrawn) A transdermal patch for administering fentanyl, comprising an adhesive fentanyl reservoir on a backing layer; said reservoir comprising a single phase polymeric composition free of undissolved components containing a polyacrylate adhesive having sufficient solubility for fentanyl to contain dissolved fentanyl in an amount sufficient to induce and maintain analgesia in a human for at least three days, said patch exhibiting a standardized C_{max} of about 0.14 to about 0.17 ng/mL/cm^2.

80. (Withdrawn) The patch of claim 78 or 79 wherein the patch exhibits a steady state drug flux of about 8.2 to 8.9 μg/cm^2/hr.

81. (Withdrawn) The patch of claim 78 or 79 wherein said reservoir comprises an amount of dissolved fentanyl sufficient to induce and maintain analgesia for about 4-14 days.

82. (Withdrawn) The patch of claim 78 or 79 wherein said reservoir comprises an amount of dissolved fentanyl sufficient to induce and maintain analgesia for about 6-8 days.

83. (Withdrawn) The patch of claim 81 wherein said adhesive is a polyacrylate adhesive having a T_g less than -10° C; and fentanyl has a solubility of about 8% by weight.

84. (Withdrawn) The patch of claim 83 wherein the reservoir has a dry coating weight of about 10 to 12 mg/cm^2.

85. (Withdrawn) The patch of claim 84 wherein the reservoir comprises about 0.84 to 3.56 mg/cm^{2}of fentanyl base.

86. (Withdrawn) The patch of claim 85 wherein the reservoir comprises about 0.84 to 1.72 mg/cm^2 of fentanyl base.

87. (Withdrawn) A monolithic transdermal patch for administering fentanyl, comprising an adhesive fentanyl reservoir on a backing layer, said reservoir comprising a single phase polymeric composition free of undissolved components containing a polyacrylate adhesive having sufficient solubility for fentanyl to contain dissolved fentanyl in an amount sufficient to induce and maintain analgesia in a human for at least three days, said patch being completely free from a rate controlling membrane, said patch exhibiting a normalized C_{max} of about 16.8 to 18.7 ng/mL-mg/hr.

88. (Withdrawn) A monolithic transdermal patch for administering fentanyl, comprising an adhesive fentanyl reservoir on a backing layer, said reservoir comprising a single phase polymeric composition free of undissolved components containing a polyacrylate adhesive having sufficient solubility for fentanyl to contain dissolved fentanyl in an amount sufficient to induce and maintain analgesia in a human for at least three days, said patch being completely free from a rate controlling membrane, said patch exhibiting a standardized C_{max} of about 0.14 to about 0.17 ng/mL/cm^2.

89. (Withdrawn) The patch of claim 87 or 88 wherein said reservoir comprises an amount of dissolved fentanyl sufficient to induce and maintain analgesia for about 6-8 days

wherein fentanyl has a solubility of about 8% by weight in said reservoir; the reservoir has a drying coating weight of about 10-12 mg/cm^2; and said patch exhibits a steady state drug flux of about 8.2 to 8.9 μg/cm^2/hr.

90. (Withdrawn) The patch of claim 87 or 88 wherein the reservoir comprises about 0.84 to 3.56 mg/cm^{2}of fentanyl base.

91. (Withdrawn) The patch of claim 55 which is pharmacologically equivalent to DURAGESIC

EVIDENCE APPENDIX

None.

RELATED PROCEEDINGS APPENDIX

None.